60th Medical Group (AMC), Travis AFB, CA

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

FINAL REPORT SUMMARY

(Please type all information. Use additional pages if necessary.)

PROTOCOL #: FDG20160011A **DATE:** 20 March 2018

PROTOCOL TITLE: A Novel Perfusion System for Damage Control of Hyperkalemia in Swine (*Sus scrofa*).

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Maj Ian Stewart

DEPARTMENT: SGSE **PHONE #:** 707-423-7264

INITIAL APPROVAL DATE: 20 June 2016 **LAST TRIENNIAL REVISION DATE:** 15 June 2017

FUNDING SOURCE: SG

1. RECORD OF ANIMAL USAGE:

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Sus scrofa	32	0	20

2. PROTOCOL TYPE / CHARACTERISTICS: (Check all applicable terms in **EACH** column)

___ Training: Live Animal ___ Medical Readiness ___ Prolonged Restraint

___ Training: non-Live Animal ___ Health Promotion ___ Multiple Survival Surgery

___ Research: Survival (chronic) ___ Prevention ___ Behavioral Study

_X_ Research: non-Survival (acute) ___ Utilization Mgt. ___ Adjuvant Use

___ Other ( ) ___ Other (Treatment) ___ Biohazard

3. PROTOCOL PAIN CATEGORY (USDA): (Check applicable) ___ C _X_ D ___ E

4. PROTOCOL STATUS:

***Request Protocol Closure:**

___ Inactive, protocol never initiated

___ Inactive, protocol initiated but has not/will not be completed

_X_ Completed, all approved procedures/animal uses have been completed

5. Previous Amendments:
List all amendments made to the protocol. **IF none occurred, state NONE. Do not use N/A.**

For the Entire Study Chronologically

Amendment Number	Date of Approval	Summary of the Change
1	15 Jul 16	Personnel
2	18 May 17	Personnel
3	30 Jun 17	Anesthetic/Analgesic/Antibiotic/Study Agent
4	20 Jul 17	Personnel
5	16 Nov 17	Personnel

6. FUNDING STATUS: Funding allocated: $32,710.00 Funds remaining: $0.00

7. PROTOCOL PERSONNEL CHANGES:

Have there been any personnel/staffing changes (PI/CI/AI/TC/Instructor) since the last IACUC approval of protocol, or annual review? _X_ Yes ___ No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.

ADDITIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, IACUC approval - Yes/No)

NAME	PROTOCOL FUNCTION	IACUC APPROVAL
Capt Harris Kashtan	AI	Yes
Capt Carl Beyer	AI	Yes
Capt Andrew Wishy	AI	Yes
Dr. Guillaume Hoareau	AI	Yes
Mrs. Lauren Walker	AI	Yes

DELETIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, Effective date of deletion)

NAME	PROTOCOL FUNCTION	DATE OF DELETION
Lt Col Timothy Williams	AI	18 May 2017
Maj Eric DeSoucy	AI	18 May 2017
Maj Robert Faulconer	AI	16 November 2017
Capt Meryl Simon-Logan	AI	18 May 2017
Capt Emily Tibbits	AI	18 May 2017

8. PROBLEMS / ADVERSE EVENTS: Identify any problems or adverse events that have affected study progress. Itemize adverse events that have led to unanticipated animal illness, distress, injury, or death; and indicate whether or not these events were reported to the IACUC.

None.

9. REDUCTION, REFINEMENT, OR REPLACEMENT OF ANIMAL USE:

REPLACEMENT (ALTERNATIVES): Since the last IACUC approval, have alternatives to animal use become available that could be substituted in this protocol without adversely affecting study or training objectives?

None.

REFINEMENT: Since the last IACUC approval, have any study refinements been implemented to reduce the degree of pain or distress experienced by study animals, or have animals of lower phylogenetic status or sentience been identified as potential study/training models in this protocol?

None.

REDUCTION: Since the last IACUC approval, have any methods been identified to reduce the number of live animals used in this protocol?

None.

10. PUBLICATIONS / PRESENTATIONS: (List any scientific publications and/or presentations that have resulted from this protocol. Include pending/scheduled publications or presentations).

Hoareau GL, Kashtan H, Walker L, Beyer C, Wishy A, Grayson JK, Ross JD, Stewart IJ. A novel perfusion system for damage control of hyperkalemia in swine. Shock (Accepted December 2017)

11. PROTOCOL OBJECTIVES: (Were the protocol objectives met, and how will the outcome or training benefit the DoD/USAF?)

We met the objectives and have demonstrated the efficacy of a novel hemoperfusion system to decrease serum potassium levels. Most interestingly, we demonstrated stark differences in plasma potassium concentration at four hours, the typical length of a standard dialysis treatment. Furthermore, while this study was not powered to detect arrhythmias, it is notable that two animals in the control arm developed potentially fatal arrhythmias compared to none in the treatment group. The extracorporeal binding cartridge did not alter mean arterial pressure, fluid, or vasopressor requirements between groups, which is substantiated by a lack of difference in lactate concentration between groups at the end of the experiment. This work serves as proof-of-concept for a novel extracorporeal method of potassium removal that could have several applications for the DoD/USAF.

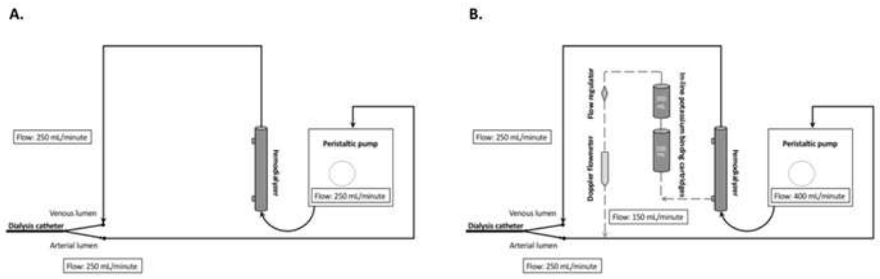
12. PROTOCOL OUTCOME SUMMARY: (Please provide, in "ABSTRACT" format, a summary of the protocol objectives, materials and methods, results - include tables/figures, and conclusions/applications.)

Objectives: The standard of care for refractory hyperkalemia is renal replacement therapy (RRT). However, traditional RRT requires specialized equipment, trained personnel, and large amounts of dialysate. It is therefore poorly suited for austere environments. We hypothesized that a simplified hemoperfusion system could control serum potassium concentration in a swine model of acute hyperkalemia.

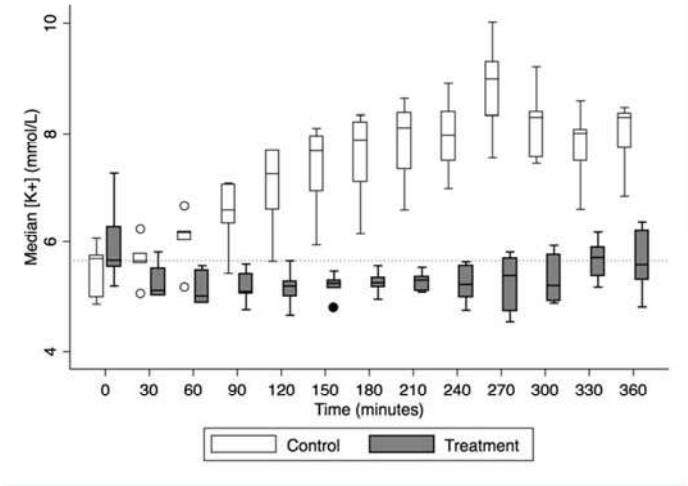
Material and methods: Ten pigs were anesthetized and instrumented. A dialysis catheter was inserted. Following bilateral nephrectomy, animals received intravenous potassium chloride and were randomized to the control or treatment group. In both groups, blood was pumped through an extracorporeal circuit (EC) with an in-line hemodialyzer. In the treatment arm, ultrafiltrate from the hemodialyzer was diverted through cartridges containing novel potassium binding beads and returned to the EC. Blood samples were obtained every 30 minutes for 6 hours.

Results: Serum potassium concentration was significantly lower in the treatment than in the control group over time ($P = 0.02$). There was no difference in serum total calcium concentration for group or time ($P = 0.13$ and 0.44, respectively) or platelet count between groups or over time ($P = 0.28$ and 1.00, respectively). No significant EC thrombosis occurred. Two of five animals in the control group and none in the treatment group developed arrhythmias. All animals survived until end of experiment.

Conclusions/applications: A simplified hemoperfusion system removed potassium in a porcine model. In austere settings, this system could be used to temporize patients with hyperkalemia until evacuation to a facility with traditional RRT.



Extracorporeal circuit diagram. **A.** Control group. **B.** Treatment group.



Comparison of median serum potassium concentration over time between control and treatment groups. The horizontal line within each box defines the median value; upper and lower limits of each box denote the interquartile range. Whiskers delineate the 5–95% range. Individual data points outside of this range are plotted as individual circles.). Serum potassium concentration was significantly lower in the treatment group when compared to the control group, and this was consistent over time ($P < 0.001$). Serum concentrations were significantly lower in the treatment compared to the control group at T210, T240, T270, and T300 ($P = 0.034$, $P = 0.01$, $P < 0.001$, $P = 0.004$, respectively). In the control group, serum potassium concentration at T240, T270, and T300 was significantly increased compared to T0 ($P = 0.048$, $P < 0.001$, and $P = 0.011$, respectively). In the treatment group, there was no significant difference in serum potassium over time. There was no significant difference in serum potassium between T0 and T360 for the treatment group; the control group had higher serum potassium at T360 compared with T0 ($p = 0.05$ for the control group, $p = 1$ for the treatment group).

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IAN STEWART, Maj, USAF, MC

24 April 2018

(Date)

Attachments:
Attachment 1: Defense Technical Information Center (DTIC) Abstract Submission **(Mandatory)**

Attachment 1

Defense Technical Information Center (DTIC) Abstract Submission

This abstract requires a brief (no more than 200 words) factual summary of the most significant information in the following format: Objectives, Methods, Results, and Conclusion.

Objectives:

The standard of care for refractory hyperkalemia is renal replacement therapy (RRT). However, traditional RRT is poorly suited for austere environments. We hypothesized that a simplified hemoperfusion system could control serum potassium concentration in a swine model of acute hyperkalemia.

Methods:

Ten pigs were anesthetized and instrumented. Following bilateral nephrectomy, animals received intravenous potassium chloride and were randomized to the control or treatment group. In both groups, blood was pumped through an extracorporeal circuit (EC) with an in-line hemodialyzer. In the treatment arm, ultrafiltrate from the hemodialyzer was diverted through cartridges containing novel potassium binding beads and returned to the EC.

Results:

Serum potassium concentration was significantly lower in the treatment than in the control group over time ($P = 0.02$). There was no difference in serum total calcium concentration for group or time ($P = 0.13$ and 0.44, respectively) or platelet count between groups or over time ($P = 0.28$ and 1.00, respectively). All animals survived until end of experiment.

Conclusion:

A simplified hemoperfusion system removed potassium in a porcine model. In austere settings, this system could be used to temporize patients with hyperkalemia until evacuation to a facility with traditional RRT.

Grant Number:_____

From:_____

****If you utilized an external grant, please provide Grant # and where the grant came from. Thank you.**